Can Ringer's Lactate Be Used Safely with Blood Transfusions?

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BACKGROUND: Blood bank recommendations specify that Ringer's lactate solution (LR) should be avoided while transfusing blood. However, there are few studies either evaluating or quantifying increased coagulation during rapid infusion of LR and blood.

DESIGN AND METHODS: Whole blood (WB, n = 25) and packed red blood cells (PRBC, n = 26) were rapidly admixed with normal saline (NS), Lactate solution and LR with 1 g (LR-1), 2 g (LR-2), and 5 g (LR-5) $CaCl_2$/L solutions for assessment of infusion time, filter weight, and clot formation.

RESULTS: No significant differences in infusion time or filter weight using WB or PRBC with NS or LR were seen. No significant difference in clot formation between NS and LR with WB or PRBC was found, but the presence of visible clot was increased in the LR-5 group ($P = 0.013$, WB, and $P = 0.002$, PRBC).

CONCLUSION: A comparison of LR and NS with rapid infusion rates of blood showed no significant difference between infusion time, filter weight and clot formation. Blood bank guidelines should be revised to allow the use of LR in the rapid transfusion of PRBC. *Am J Surg.* 1998;175:308–310. © 1998 by Excerpta Medica, Inc.

Under current blood bank guidelines, only normal saline (NS) solution (0.9% NaCl USP) may be administered with blood components.[1–3] Storage of blood, for transfusion, requires the addition of citrate-phosphate-dextrose (CPD) solution, which contains the active compound sodium citrate. This compound prevents blood coagulation by chelating the calcium ion and thus disrupting the coagulation cascade.[2,4] Theoretically, the danger of infusing Ringer's lactate solution (LR) with the blood transfusion is that the calcium in LR will exceed the chelating capabilities of the citrate in the stored blood, resulting in clot formation.[5,6] These clots could then enter the circulation and compromise the microcirculation, particularly the pulmonary capillaries and small vessels.[7]

Several studies have shown that small fibrin clots may be produced in the intravenous tubing if LR is infused at the same time as the blood transfusion at slow rates.[5,6] Clot formation in the intravenous tubing increases as the rate of infusion decreases and ambient temperature increases.[5,6] However, these studies have not measured clot formation at the high infusion rate commonly used during a standard trauma resuscitation.

Our hypothesis is that there is no difference in clot formation between NS and LR while transfusing blood at a rapid infusion rate. To test this hypothesis, we evaluated filter clot formation, filter weights, and infusion times using NS, LR, and LR solutions with additional calcium chloride.

MATERIALS AND METHODS

Units of whole blood (WB) and packed red blood cells (PRBC) of several ABO types were used. The duration of storage was between 15 and 30 days, which is the most common blood available in the trauma field. The units of blood ranged were anticoagulated using CPD as established by the blood bank guidelines.[1–3] The study was separated into five different experimental groups, and in each specific group the blood was transferred separately into pediatric "quad packs" (100 mL each) at room temperature. Each quad pack was then mixed separately with a 100 mL aliquot of NS, used as the control solution, LR, or LR solution with additional calcium chloride at 1 g/L (LR-1), 2 g/L (LR-2), and 5 g/L (LR-5). The citrate:calcium ratios and the number of trials per solution are shown in **Tables I and II**.

Using standard blood filter tubing with a 170 micron filter (McGaw Inc., Irvine, California), each mixture of WB or PRBC and crystalloid solution was infused immediately after mixing using gravity flow from an elevation of 30 inches above a collection reservoir. For each mixture, a new blood filter tubing was used. The infusion time of each mixture was recorded in seconds, and the micropore filter weight was determined and recorded in grams as soon as the infusion was finished. Data are presented as the mean ± standard error of the mean. The group means were analyzed with paired *t* test and analysis of variance (ANOVA), using NS as the control group. The appearance of gross clot in the filter was recorded and analyzed using chi-square and/or Fischer's exact test. Significance was attributed to a P value <0.05.

RESULTS

The investigations were performed using 25 units of WB and 26 units of PRBC, with all 5 crystalloid solutions used for each blood group (Table I).

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TABLE I
Citrate:Calcium Ratios for Whole Blood and Packed Red Blood Cells

	N*		Ratio†	
Solution	W	P	W	P
NS	25	26	—	—
LR	25	26	4.0	13.0
LR-1	17	18	0.8	0.25
LR-2	17	18	0.4	0.13
LR-5	16	16	0.165	0.05

** Number of samples in each group.*
† Micromoles citrate:micromoles calcium.
W = whole blood; P = packed red blood cells; NS = normal saline; LR = Ringer's lactate solution.

In the WB group, there was no difference in infusion times among NS, LR, and the calcium-enriched LR solutions (Table II). In the PRBC group, there was a statistically significant increase in infusion time between NS and the LR-5 solution ($P < 0.001$; Table II).

In the WB group, no significant difference in filter weight was found between NS and LR, but filter weight was significantly increased with LR-1 ($P = 0.006$) and LR-2 ($P < 0.001$; Table II). In the PRBC group, there was a trend toward increased filter weight as additional amounts of calcium were added, but this was not statistically significant (Table II).

There was some gross clot formation in the filter in both the WB and the PRBC groups with all the solutions. There was no statistically significant difference in the incidence of clot formation between NS and LR in either the WB or the PRBC groups (**Table III**). The appearance of gross clot was significantly increased using LR-5 versus NS in both WB ($P = 0.013$) and PRBC ($P < 0.001$; Table III).

The group means were examined with ANOVA. The difference in mean times between mixtures of PRBC is statistically significant with a P value of 0.004. The difference in mean weights within this group is also statistically significant, $P = 0.012$. While the comparison of mean times for the WB group is not statistically significant ($P = 0.059$), the differences among mean weights are ($P < 0.001$).

COMMENTS

During trauma resuscitation, LR has proven to be an excellent initial intravenous fluid therapy due to its isotonicity and few side effects.[8] Previous investigations have proven that the use of blood plus LR to treat hemorrhagic shock in animals and humans results in a more rapid return to cardiovascular stability, correction of acidosis, and decreased mortality than does treatment with either blood alone or any other type of crystalloid solution.[9,10] In clinical practice, LR has been administered during trauma resuscitation not only before, but also between blood transfusions without reported clinical complications.[10]

Blood bank recommendations state that normal saline solution should be used instead of LR while transfusing blood to increase the infusion rate and decrease the viscosity of PRBC.[1–3] This recommendation is based on investigations demonstrating that calcium-containing solutions can initiate in vitro coagulation in citrated blood.[5,6] LR contains 0.020 g $CaCl_2$ per liter of solution. A unit of WB contains approximately 63 mL CPD or 1.66 g citrate, and one unit of PRBC contains approximately 0.520 g citrate. Ryden and Oberman[5] demonstrated that trace amounts of clot could be obtained from intravenous tubing at a whole blood to LR volume ratio of 1:1 at room temperature. Fibrin clots were seen when the flow rate was slow (60 drops per minute). In that study, gross clot formation was observed at a blood:LR volume concentration of 1:5 at a temperature of 37°C. They concluded that clot formation may be produced more frequently than expected when blood is transfused with LR in situations where the flow is slow and the ambient temperature is high.[5]

Other studies have demonstrated no significant difference in clot formation between PRBC diluted with LR compared with PRBC diluted in NS. One study demonstrated no difference in filter weights when comparing PRBC diluted in LR versus NS when they were transfused through a filter at 540 mL/hr.[11] Cull et al[12] showed that there was no significant clot formation with the dilution of PRBC and LR at clinically relevant levels (5:1, 3:1, and 2:1). Another study showed that no significant difference in microaggregate numbers or size was found when red blood cells were reconstituted with NS versus LR.[13]

This investigation was designed to simulate the conditions in a trauma resuscitation with "wide open" intrave-

TABLE II
Infusion Times and Filter Weights for Whole Blood and Packed Red Blood Cells

Solution		Infusion Time (seconds)	*P* Value	Filter Weight (grams)	*P* Value
NS	W	110.8 ± 4.0	—	13.2 ± 0.3	—
	P	109.4 ± 3.6	—	13.6 ± 0.4	—
LR	W	106.2 ± 3.6	0.300	14.5 ± 0.6	0.054
	P	116.6 ± 4.7	0.229	13.1 ± 0.3	0.286
LR-1	W	115.2 ± 5.2	0.300	16.3 ± 0.9	0.006
	P	108.3 ± 8.4	0.300	15.1 ± 0.7	0.062
LR-2	W	120.4 ± 5.2	0.153	16.3 ± 0.6	<0.001
	P	104.2 ± 4.1	0.300	14.2 ± 0.6	0.300
LR-5	W	103.3 ± 3.1	0.147	12.7 ± 0.3	0.204
	P	132.9 ± 4.1	<0.001	12.9 ± 0.4	0.200

W = whole blood; P = packed red blood cells; NS = normal saline; LR = Ringer's lactate solution.

TABLE III
Clot Formation in Whole Blood and Packed Red Blood Cells

	N*		Percent†		*P* Value	
Solution	W	P	W	P	W	P
NS	25	26	24	11	—	—
LR	25	26	20	15	0.733	0.687
LR-1	17	18	29	16	0.698	0.632
LR-2	17	18	35	16	0.568	0.632
LR-5	16	16	62	56	0.013	0.002

** Number of samples in each group.*
† Percentage of samples that clotted.
W = whole blood; P = packed red blood cells; NS = normal saline; LR = Ringer's lactate solution.

nous infusion rates of blood and crystalloid solutions at room temperature. Under these "real life" conditions, there was no significant increase in infusion time, filter weight, or gross blood clot formation using LR versus NS. This is consistent with previous investigations in which no difference was found between LR and NS in the flow rates at any hematocrit level.[12]

This study demonstrates that LR does not cause increased coagulation versus NS at a blood:crystalloid volume ratio of 1:1 during a blood transfusion at a rapid infusion rate. Further, under these conditions an extraordinary amount of $CaCl_2$ (5 g/L) would have to be added to LR before clinically significantly increased clotting would occur at these infusion rates.

During trauma resuscitations, the patients require intensive management, with multiple procedures and interventions being simultaneously performed. The need to change intravenous solution bags from LR to NS to comply with blood bank guidelines at this critical period is time consuming for the trauma team. This time and effort could be better directed to other critical aspects of the resuscitation. Based on this and other data, blood bank recommendations should be amended to allow the use of LR with the transfusion of PRBC at rapid infusion rates.

REFERENCES

1. American Association of Blood Banks. *Blood Transfusion Therapy*. 1st ed. Arlington: American Association of Blood Banks; 1983.
2. Widman FK, ed. *Technical Manual*. 11th ed. Arlington: American Association of Blood Banks; 1993.
3. American Association of Blood Banks. *Accreditation Requirements Manual*. 5th ed. Arlington: American Association of Blood Banks; 1994.
4. Beutler E, Masouredis SP. Preservation and clinical use of erythrocytes and whole blood. In: Williams WJ, ed. *Hematology*. New York: McGraw-Hill; 1995:1622–1627.
5. Ryden SE, Oberman HA. Compatibility of common iv solutions with cpd blood. *Transfusion*. 1975;15:250–255.
6. Dickson DN. Compatibility of blood with solutions containing calcium. *S Afr Med J*. 1980;57:785–787.
7. Connell RS, Swank RL. Pulmonary microembolism after blood transfusions. *Ann Surg*. 1973;177:40.
8. American College of Surgeons Committee on Trauma. Initial assessment and management. In: *American College of Surgeons Committee on Trauma: Advanced Trauma Life Support Program*, Chicago, 1993:25.
9. Canizaro PC, Praguer MD, Shires GT. The infusion of Ringer's lactate solution during shock. *Ann J Surg*. 1971;122:494.
10. James PE, Bredenberg CE, Collins JA, et al. Tolerance of lactate infusion by wounded in hemorrhagic shock. *Ann Surg*. 1972;38:124–129.
11. King WH, Patten ED, Bee DE. An in vitro evaluation of ionized calcium levels and clotting in red blood cells diluted with lactated Ringer's solution. *Anesthesiology*. 1988;68:115–121.
12. Cull DL, Lally KP, Murphy KD. Compatibility of packed erythrocytes and Ringer's solution. *Surg Gynecol Obstet*. 1991;173:9–12.
13. Barkhoff RL, Gavin M, Hickey TM, et al. Compatibility of packed red blood cells with Ringer's lactate or plasmalyte A. *Clin Res*. 1984;32:33. Abstract.